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EXAMINER	
GANSHEROFF, L	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No. 09/600,027	Applicant(s) TANABE ET AL.	
	Examiner Lisa Gansheroff	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133)..
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07/11/00-09/06/00* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☒ Claim(s) *1-13* is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .

18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Pending claims: 1-13.

Response to: Preliminary Amendments filed 11 July, 2000 and 06 September 2000.

It is noted that the Examiner has reviewed the references that were provided with the International Search Report.

Specification

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Sequence compliance

Acknowledgement is made of the receipt of a paper copy and computer readable form of the sequence listing and of the Applicant's statement that these are the same and contain no new matter. The sequence listing from the computer readable form has been entered.

Claim Objections

Claims 1-13 are objected to because of the following informalities:

In claim 1, it is suggested that "much" in line 2 be replaced with "many", and that the work "a" be inserted between the words "of" and "cell" in line 3 of the claim.

In claim 4, it appears that the word "of" is missing between the words "method" and "mutation" in line 1 of the claim.

Appropriate correction is required.

Claims 9 and 10 are objected to under 37 CFR 1.75(c), as being of improper dependent

form for failing to further limit the subject matter of a previous claim. Claim 9 depends from any one of claims 1-8 or 11-13, and claims 11-13 are not previous claims. Applicant may cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9 and 10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a genus of cells of any type and any mutated gene isolated from said cells. The Written Description rejection is thus based on several factors. First, since the word "gene" refers not only to a coding sequence but also to an entire genomic structure (including introns and all regulatory regions upstream and downstream of coding sequences), and since the entire genomic structure of a representative number of eukaryotic "genes" is not known, claim 10 is subject to a rejection for an inadequate written description based on this terminology, as it encompasses any eukaryotic genes. Second, the species of mutated cells and

genes of claims 9 and 10 are highly variant. Mutated cells and genes can function very differently from wild-type cells very differently from each other. Each mutated gene has a different sequence, and Applicants are not in possession of a representative number of isolated mutated genes from any organism. A description of a method of mutagenesis is not a description of either the structure or the function of a mutated gene or a mutated cell. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the sequence of a few *E. coli* mutations alone is insufficient to describe the genus of mutant cells and isolated mutated genes. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claims 1, 9, and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using a mutator gene (a gene defective in mismatch repair) for the method, does not reasonably provide enablement for any other means of introducing more mutations into one genomic DNA strand than another. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The following factors have been considered in determining that the specification does not enable the skilled artisan to practice the invention commensurate in scope with the claims.

The nature of the invention. The invention is complex, because it requires introducing mutations into genomic DNA of any organism such that many more point mutations are

introduced into one strand than into the other strand.

The state of the prior art and the predictability or unpredictability of the art. The prior art teaches that mutations occur during DNA replication, and teaches that these mutations occur preferentially in one strand (see for example Iwaki et al. 1996. Mol. Gen. Genet. 251:657-664, and Fijalkowska et al. 1998. Proc. Natl. Acad. Sci. USA 95:10020-10025). Thus, when there is a mutation in a DNA polymerase subunit that increases the mutation rate based on deficient proofreading activity during replication, or a mutation in a gene involved in mismatch repair such that errors from replication are not repaired, the increased number of mutations will occur more in one strand than another. However, the Examiner has not found in the art a teaching of another means, aside from the use of mutator genes, of obtaining more mutations in one strand than the other. Thus, it is unpredictable how one would achieve such mutagenesis without the use of mismatch-repair mutators.

The amount of direction or guidance presented in the specification and the presence or absence of working examples. The specification and working examples are limited to mutagenesis with the temperature-sensitive mutator *dnaQ49*. There is no guidance as to how to effect more mutations in one strand than another in a way that does not use mutator genes that are defective in mismatch repair.

The breadth of the claims. The claims are very broad, encompassing mutagenizing one strand preferentially in ways that do not involve the use of mutators in mismatch-repair, and encompassing such mutagenesis in any organism.

The quantity of experimentation. Based on the complexity of the invention, the state of the prior art and unpredictability of the prior art, the lack of guidance and working examples in

the specification with respect to non-mutator gene methods, and the breadth of the claims, an undue amount of experimentation is required for one of skill in the art to practice the claimed invention commensurate with its scope.

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for introducing many more point mutations into one strand of double-stranded genomic DNA of a cell in which strand-specific differences in replication fidelity and mutators have been characterized, does not reasonably provide enablement for this mutagenesis method in other "organism individuals", for example higher (multicellular) eukaryotes, such as mammals or Drosophila. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The following factors have been considered in determining that the specification does not enable the skilled artisan to practice the invention commensurate in scope with the claims.

The nature of the invention. The invention is very complex, because it encompasses making many more point mutations in one strand of genomic DNA not only in well-characterized organisms such as *E. coli*, but also in very complex less-characterized organisms such as mammals.

The state of the prior art and the predictability or unpredictability of the art. With respect to higher eukaryotes, such as mammals, while genes have been identified that increase spontaneous mutation frequency, such as some genes associated with cancers, the Examiner has

been unable to find prior art teaching that mutagenesis by mutators in mammals or other higher eukaryotes is associated with many more mutations in one strand of genomic DNA than another, or that replication of genomic DNA shows less fidelity on one strand than another. Iwaki et al. (1996) mention some studies with HeLa cell extracts, but note that these were with respect to Simian virus 40 origins, not mammalian genomic DNA.

The amount of direction or guidance presented in the specification and the presence or absence of working examples. There is no guidance presented in the specification for how to practice the method except with a well-characterized *E. coli* mutator, and the only working examples are in *E. coli* with the *E. coli dnaQ49* mutator. There is also no guidance as to how to introduce mutations in this way without the use of mismatch-repair gene mutators.

The breadth of the claims. The claims are very broad, encompassing mutagenesis methods with entire eukaryotic organisms, such as mice or even primates.

The quantity of experimentation. Based on the following: the complexity of the invention; the lack of teachings in the prior art to direct one as to whether genomic DNA replication and known mutators in organisms such as mammals would enable introducing many more point mutations on one strand of genomic DNA than another; the absence of guidance or working examples in the specification with respect to practicing the method with any organism except *E. coli*; and the breadth of the claims, an undue amount of experimentation is required for one of skill in the art to practice the claimed invention commensurate with its scope.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 , 9, and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Fijalkowska et al. (1998. Proc. Natl. Acad. Sci. USA 95:10020-10025).

Fijalkowska et al. teach that there is unequal fidelity of leading strand and lagging strand DNA replication on the *E. coli* chromosome; that is there are more mutations introduced in one strand of double-stranded genomic DNA than another. Mutations were introduced into a *lacZ* gene using a *mutL* mutator gene, a *mutD5* mutator gene, or a *dnaQ49* mutator gene. In these strains, mutations were introduced more in one strand than another, and the mutations involved both transitions and transversions and were in four kinds of bases. These teachings meet the limitations of claims 1-4 and 9. See for example p. 10023. Additionally, to construct the starting strains for the mutator mutagenesis, Fijalkowska et al. used isolated mutated *lacZ* genes (these mutations were used to screen for other mutations introduced by the mutators). See page 10021. These isolated mutated *lacZ* genes meet the limitations of claim 10.

Claims 1-4 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Lin et al. (U.S. Patent 5,348,872).

Lin et al. teach a method for isolating mutant cells and mutant cells isolated by the

method. Lin et al. teach that the method can comprise the use of mutator genes, such as *mutD* (which is the same gene as *dnaQ*; see Fijalkowska et al., page 10023, right column). The mutations are introduced into the genomic DNA of any cell or organism individual. The reason for the use of the mutator gene is to increase the frequency of mutations. The cells are under a selection load condition, in that in order for the cell to grow well and be selected, it must acquire a mutation that allows it to perform a certain function (that function being increased secretion of a particular compound). Inherent in the method of Lin et al. is that the mutated gene can be isolated from the mutant cell for analysis.

Since the mutator *mutD* is used (see Example 1 in column 9), inherent in the method is that many more mutations are introduced in one strand of genomic DNA than the other. Thus, although Lin et al. do not teach this as a mechanism for their mutagenesis method, the method steps are the same as those of the instant claims. See columns 1-5 and column 9.

Claims 9 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Pan et al. (1996. Antimicrobial Agents and Chemotherapy 40:2321-2326).

Pan et al. teach ciprofloxacin-resistant mutants of *Streptococcus pneumoniae* that were generated by stepwise selection at increasing drug concentrations; the mutations are in genomic DNA. Pan et al. teach mutant cells or organism individuals, and Pan et al. teach mutated genes isolated from mutant cells (see abstract; page 2321, last paragraph before the Materials and Methods section, and pages 2322-2323). The patentability of a product does not depend on its method of production; thus the teachings of the reference meet the limitations of the claims.

Claims 9 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Garza et al. (1995. Proc. Natl. Acad. Sci. USA 92:1970.).

Garza et al. teach mutant cells and isolated mutated genes; the mutations are in the motA gene. See page 1971, left column, third full paragraph, page 1973, first full paragraph, and page 1970. The patentability of a product does not depend on its method of production; thus the teachings of the reference meet the limitations of the claims.

Claims 9 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Herbst et al. (1994. Proc. Natl. Acad. Sci. USA 91:12525-12529).

Herbst et al. teach a mutant cell and an isolated mutated gene; the gene encodes the ribosomal protein L9. See page 12525 and page 12526 right column. The patentability of a product does not depend on its method of production; thus the teachings of the reference meet the limitations of the claims.

Claims 9 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Ota et al. (1992. Proc. Natl. Acad. Sci. USA 89:2355-2359).

Ota et al. teach a mutant cell and an isolated mutated gene. The gene is called the *PTP2* gene. See page 2355 and page 2356, right column. The patentability of a product does not depend on its method of production; thus the teachings of the reference meet the limitations of the claims.

Claims 9 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Sussel et al. (1991. Proc. Natl. Acad. Sci. USA 88:7749-7753). Sussel et al. teach a mutant cell and an isolated mutated gene; the gene is called *RAP1*. See page 1149 and page 7750 first full paragraph in the left column. The patentability of a product does not depend on its method of production; thus the teachings of the reference meet the limitations of the claims.

It is noted that regarding claims 9 and 10, since the patentability of a product does not depend on its method of production (see MPEP 2113), the claims read on any mutant cell and on any isolated mutated gene (with a point mutation). It would be impractical and impossible to present in an Office Action a comprehensive list of art rejections over every prior art reference that teaches a mutant cell or an isolated mutated gene.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6 and 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fijalkowska et al., as applied to claims 1-4 and 9 above in view of Lin et al., as applied to claims 1-4, 9, and 10 above, and further in view of either Imamoto et al. (U.S. Patent 5,928,866), or, alternatively, Iwaki et al. (1996. Mol. Gen. Genet. 251:657-664).

Fijalkowska et al. teach a method for mutagenesis and teach that more mutations are introduced into one strand of genomic DNA than another, and teaches mutators in mutation-repair gene group (*dnaQ, dnaE, mutL, mutH, and mutS*; see for example p. 10020), and teaches mutant cells whereby the mutations were introduced by a method using a mutator. Fijalkowska et al. use the *dnaQ49* temperature-sensitive mutation at the temperature (certain condition) at which it causes more mutations (37°C), although Fijalkowska et al. do not review that dnaQ49 is a temperature-sensitive mutator. Fijalkowska et al. also do not teach a selection load or isolation of the mutated gene.

Lin et al. teach a method for isolating mutant cells and mutant cells isolated by the method. Lin et al. teach that the method can comprise the use of mutator genes, such as mutD (which is the same gene as *dnaQ*; see Fijalkowska et al., page 10023, right column). The mutations are introduced into the genomic DNA of any cell or organism individual. The reason for the use of the mutator gene is to increase the frequency of mutations. Lin et al. teach that mutator genes can increase the mutation rate of a cell by between 1000-100000-fold, and Lin et

al. also caution that mutators can result in mutation of genes other than those of interest (see column 5, lines 3-23). The cells are under a selection load condition, in that in order for the cell to grow well and be selected, it must acquire a mutation that allows it to perform a certain function (that function being increased secretion of a particular compound). Since a mutator such as mutD is used, inherent in the method is that many more mutations are introduced in one strand of genomic DNA than the other. Thus, although Lin et al. do not teach this as a mechanism for their mutagenesis method, the method steps are the same as those of the instant claims. See columns 4-5 and column 9. Lin et al. do not teach a mutator gene which causes a defect under a certain condition.

Imamoto et al. teach a method for preparing mutant genes on plasmids which comprises using host cells lacking DNA error-correcting function, and that the plasmid construction takes into account different mutagenesis rates on different strands of DNA; see abstract and columns 1-3. The examples use *dnaQ49*, a mutator which causes a defect of mutation repair under a certain condition (a certain temperature); see for example columns 3-5. Imamoto et al. do not teach mutagenesis of genomic DNA.

Iwaki et al. teach that *dnaQ49* is a temperature-sensitive mutation that increases the frequency of mutations, and that more mutations are introduced into one strand of double-stranded plasmid DNA than another. Iwaki et al. do not teach mutagenesis of genomic DNA.

At the time of the invention of the instant application, one of ordinary skill in the art would have been motivated to isolate mutations in genomic genes as a way to study the function of such genes or to identify genes that perform certain functions. One would have been motivated to use a mutator strain defective in mismatch-repair, as suggested by Lin et al., and a

selection load condition. Further, since Lin et al. note that mutators could mutate other genes in the cell in a way that would be undesirable for the mutagenesis, one would have been motivated to modify the method of Lin et al. to limit the number of background mutations, especially since one would not have been able to predict in advance, for every situation, which background mutations would be particularly undesirable (aside from those causing death of the cell) and how to avoid getting those mutations accidentally. One would have thus been motivated use a mutator known in the art that is defective under a certain condition, such as the *dnaQ49* taught by Iwaki et al. In this way, mutations could be introduced for a defined period of time under the certain condition, and then the cell could be removed from that certain condition so that a high frequency of mutations did not continue to form indefinitely and possibly kill the cell or complicate genetic analysis by the existence of a variety of different mutations in the cell. It also would have been obvious to isolate a mutated gene from the mutant cell to see what gene was mutated and to determine the sequence of the mutation for further analysis. Success would have been expected.

Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fijalkowska et al. and Lin et al., in view of either Imamoto et al. or Iwaki et al., as applied to claims 1-6 and 9-12 above, and further in view of Pan et al (1996. Antimicrobial Agents and Chemotherapy 40:2321-2326).

Fijalkowska et al. teach mutagenesis by using a mutator gene in a mismatch repair gene group so that more mutations are introduced into one strand of genomic DNA than another, and Fijalkowska et al. teach mutant cells. Fijalkowska et al. do not teach a selection load or isolation

of a mutated gene.

Lin et al. teach a mutagenesis method using a mutator gene in a mismatch repair gene group, which inherently introduces more mutations into one strand of genomic DNA than another; see above. Lin et al. do not teach a certain condition for the mutator gene or a selection load condition.

Iwaki et al. teach that dnaQ49 is a temperature-sensitive mutation that increases the frequency of mutations. Iwaki et al. do not teach mutagenesis of genomic DNA.

Pan et al. teach ciprofloxacin-resistant mutants of *Streptococcus pneumoniae* that were generated by stepwise selection at increasing drug concentrations; the mutations are in genomic DNA. Pan et al. teach mutant cells or organism individuals. Different concentrations of drug were tested at each step, and some "fourth-step" mutants were isolated with the same selection load (drug concentration) as the third-step mutants (see page 2322, right column, and page 2323). Pan et al. also teach that mutants from mutagenesis methods where the steps were repeated had resistance to higher levels of the ciprofloxacin and had more mutations, and that there are primary and secondary target genes for mutations that lead to resistance (see summary in Abstract). Pan et al. note that the presence of mutations in different targets has implications regarding chemotherapy and approaches to minimize the emergence of clinical resistance (see page 2325, right column). Pan et al. also review isolated mutated genes that they had studied previously that caused resistance to ciprofloxacin (page 2321, right column). Pan et al. do not teach the use of mutator genes, but since the mutations are apparently spontaneous mutations, it is reasonable that at least some of them were due to mutations in replication, which, as discussed above, inherently introduces more mutations into one strand than another. Pan et al. also do not

teach a certain condition for the mutator gene, such as temperature-sensitivity.

At the time of the invention of the instant application, one of ordinary skill in the art would have been motivated to perform mutagenesis to isolate mutant cells and mutated genes to study the function of the mutated genes for various purposes, such as identifying what genes can be targets for antibiotics, since such studies have clinical implications. Other studies would also have benefited from mutagenesis to identify genes important in other cellular processes. It would have been obvious to use a mutator gene to increase the frequency of mutations to expedite the studies, as taught by Lin et al., but it would have been obvious to use a mutator gene that caused a high frequency of mutations only under a certain condition, such as the *dnaQ49* mutation reviewed by Iwaki et al., in order to have minimized excessive mutations that could have lead to cell death, or that could have complicated studies of a particular mutation. It would also have been obvious to the ordinary artisan to have used a selection load and to have repeated the mutagenesis steps using increasing selection loads as taught by Pan et al. Routine experimentation would have dictated exactly what selection loads at each step would have been optimal, for example, for isolating mutants with increased resistance to an antibiotic based on the cells growth in the presence of the antibiotic at the previous step. Pan et al. teach some steps in which the increased selection load was not identical to that of the previous step, and other steps in which the selection load was the same as that of the previous step, although the optimization was not exhaustive in the case of Pan et al. Since growth under the selection load condition would have allowed for more mutations to occur with a mutator gene, and since too many mutations would have complicated the studies or have been deleterious, it would have been obvious to remove cells from the "certain condition" in which mutations were introduced before

placing the cells in the new selection load condition. Success would have been expected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa J. Gansheroff whose telephone number is (703) 605-1203. The examiner can normally be reached 9 AM - 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Richard Schwartz can be reached at (703) 308-1133. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242 for regular communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst Dianiece Jacobs whose telephone number is (703) 305-3388 or to the receptionist whose telephone number is (703) 308-0196.

LG
February 23, 2001

Remy Yucel

REMY YUCEL, PH.D
PRIMARY EXAMINER